

## SUPPLEMENTAL AMENDMENT &amp; RESPONSE UNDER

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Serial No.: 09/634207

Filed: August 9, 2000

Title: INDOLE COMPOUNDS USEFUL FOR THE TREATMENT OF CANCER

IN THE CLAIMS

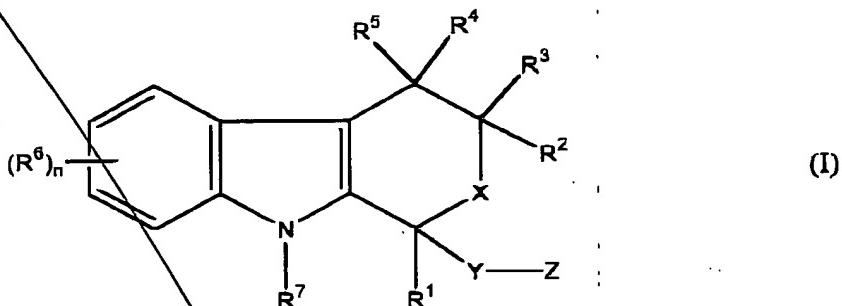
Please amend the claims as follows:

Please ass claim 49, amend claims 10, 12, 13, 14, 15, 17, 18, and 19 and cancel claim 11 without prejudice. Applicants reserve the right to pursue the cancelled subject matter in a continuing application.

Claims 1-9 (Cancelled).

*Please enter  
or  
1/13/00*

10. (Previously Amended) A method of inhibiting the viability of treating leukemia, multiple myeloma or prostate cancer cells in a mammal comprising administering an effective amount of a compound of formula (I):



*Sub E1*

wherein R<sup>1</sup> is lower alkyl, lower alkenyl, (hydroxy)lower alkyl, lower alkynyl, phenyl, benzyl or 2-thienyl, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are the same or different and are each hydrogen or lower alkyl; each R<sup>6</sup> is individually hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo, n is 1-3, R<sup>7</sup> is hydrogen, lower alkyl or lower alkenyl, X is oxy or thio, Y is carbonyl, (CH<sub>2</sub>)<sub>1-3</sub>, (CH<sub>2</sub>)<sub>1-3</sub>SO<sub>2</sub> or (CH<sub>2</sub>)<sub>1-3</sub>C(O), and Z is ( $\omega$ -(4-pyridyl)(C<sub>2</sub>-C<sub>4</sub>alkoxy), ( $\omega$ -((R<sup>8</sup>)(R<sup>9</sup>) amino)(C<sub>2</sub>-C<sub>4</sub>alkoxy), wherein R<sup>8</sup> and R<sup>9</sup> are each H, (C<sub>1</sub>-C<sub>3</sub>)alkyl or, together with N, are a 5- or 6-membered heterocyclic ring having 1-3 N(R<sup>8</sup>), S or nonperoxide O; an amino acid ester of ( $\omega$ -(HO)(C<sub>2</sub>-C<sub>4</sub>))alkoxy, N(R<sup>8</sup>)CH(R<sup>8</sup>)CO<sub>2</sub>H, 1'-D-glucuronyloxy, OH, (C<sub>2</sub>-C<sub>4</sub>)acyloxy, SO<sub>3</sub>H, PO<sub>4</sub>H<sub>2</sub>, N(NO)(OH), SO<sub>2</sub>NH<sub>2</sub>, PO(OH)(NH<sub>2</sub>), OCH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>3</sub><sup>+</sup>,

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*Sub E1*

amino, lower alkylamino, di(lower alkyl)amino, phenylamino, or tetrazoyl; or a pharmaceutically acceptable salt thereof; to a mammal afflicted with leukemia, multiple myeloma or prostate cancer.

*C1*

11. (Cancelled)

*2*

12. (Amended) The method of claim 10 or 11 wherein the treatment is for cancer is prostate cancer.

*Sub E1*

*3*

13. (Amended) The method of claim 10 or 11 wherein the treatment is for cancer is multiple myeloma.

*4*

14. (Amended) The method of claim 10 or 11 wherein the treatment is for cancer is chronic lymphocytic leukemia.

*5*

15. (Amended) The method of claim 10 or 11 wherein the [composition] is administered orally.

*6*

16. (Original) The method of claim 15 wherein an enterically coated dosage form is administered.

*7*

17. (Amended) The method of claim 10 or 11 wherein the compound of formula (I) composition is administered parenterally.

*8*

18. (Amended) The method of claim 10 or 11 wherein the compound of formula (I) composition is administered in combination with a chemotherapeutic agent.

*9*

19. (Amended) The method of claim 12 wherein the compound of formula (I) composition is administered in combination with a chemotherapeutic agent.

*3 1*

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10 26. (Previously Amended) The method of claim 18 wherein the chemotherapeutic agent is mitoxantrone, prednisone, estramustine, melphalan, vinblastine or a combination thereof.

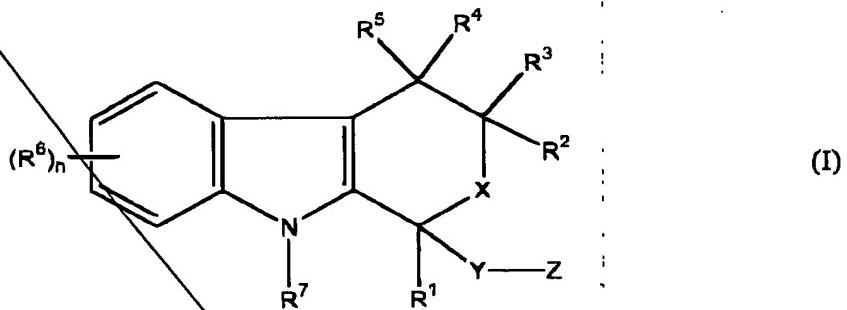
11 21. (Previously Amended) The method of claim 19 wherein the chemotherapeutic agent is an anti-androgen.

Sub 22. The method of claim 21 wherein the anti-androgen is bicalutamide, nilutamide, flutamide, cycloproterone acetate or a combination thereof.

12 23. The method of claim 21 wherein the anti-androgen is leuproide acetate, goserelin acetate or a combination thereof.

Claims 24-48 (Cancelled).

D 24. (New) A method of treating hematopoietic cancers, cancers of the bone marrow, [cancers of the colon] and cancers that express high levels of PPAR- $\gamma$  in a mammal comprising administering an effective amount of a compound of formula (I):



wherein R<sup>1</sup> is lower alkyl, lower alkenyl, (hydroxy)lower alkyl, lower alkynyl, phenyl, benzyl or 2-thienyl, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are the same or different and are each hydrogen or lower alkyl; each R<sup>6</sup> is individually hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo, n is 1-3, R<sup>7</sup> is

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*CR*  
*Sub*  
*E3*

hydrogen, lower alkyl or lower alkenyl, X is oxy or thio, Y is carbonyl,  $(CH_2)_{1-3}$ ,  $(CH_2)_{1-3}SO_2$  or  $(CH_2)_{1-3}C(O)$ , and Z is ( $\omega$ -(4-pyridyl)(C<sub>2</sub>-C<sub>4</sub>alkoxy), ( $\omega$ -((R<sup>8</sup>)(R<sup>9</sup>) amino)(C<sub>2</sub>-C<sub>4</sub>alkoxy), wherein R<sup>8</sup> and R<sup>9</sup> are each H, (C<sub>1</sub>-C<sub>3</sub>)alkyl or, together with N, are a 5- or 6-membered heterocyclic ring having 1-3 N(R<sup>8</sup>), S or nonperoxide O; an amino acid ester of ( $\omega$ -(HO)(C<sub>2</sub>-C<sub>4</sub>))alkoxy, N(R<sup>8</sup>)CH(R<sup>8</sup>)CO<sub>2</sub>H, 1'-D-glucuronyloxy, OH, (C<sub>2</sub>-C<sub>4</sub>)acyloxy, SO<sub>3</sub>H, PO<sub>4</sub>H<sub>2</sub>, N(NO)(OH), SO<sub>2</sub>NH<sub>2</sub>, PO(OH)(NH<sub>2</sub>), OCH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>3</sub><sup>+</sup>, amino, lower alkylamino, di(lower alkyl)amino, phenylamino, or tetrazolyl; or a pharmaceutically acceptable salt thereof; to a mammal afflicted with hematopoietic cancer, cancer of the bone marrow, cancer of the colon, and cancer that expresses a high level of PPAR- $\gamma$ .

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